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| 20350 7590 09/12/2008 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834 | | | | |
| EXAMINER | | | | |
| HYUN, PAUL SANG HWA | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1797 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/602,489

Applicant(s)

MANGER ET AL.

Examiner

PAUL S. HYUN

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 and 18-37 is/are pending in the application.
- 4a) Of the above claim(s) 1-13, 32 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14, 15, 18-31 and 34-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/23/08
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

REMARKS

Claims 1-15 and 18-37 remain pending with claims 1-13, 32 and 33 being withdrawn pursuant to a restriction requirement.

The IDS filed by applicant on May 23, 2008 has been acknowledged.

Despite Applicant's arguments with respect to the art rejections, the rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims **14, 15, 18-26, 28-31 and 34-37** are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. (US 2003/0008411 A1) in view of Quake et al. (US 2002/0037499 A1).

Van Dam et al. disclose a microfluidic device and a method for synthesizing a library of compounds by using the microfluidic device (see claim 15), which includes DNA synthesis (see [0056]). The device comprises a solid substrate layer and an elastomeric layer attached to the solid substrate wherein the surface of the solid substrate is immobilized with ligands for binding analytes of interest. The surfaces of both layers can comprise grooves/wells to define a plurality of first flow channels

intersecting a plurality of second flow channels (see claim 24 and [0048]). The device further comprises a plurality of control channels associated with each of the flow channels. Upon the application of an actuation force within the control channels, the elastic surface of the control channels deflect into the flow channels and block fluid flow through the flow channels. The control channels also act as a pump for facilitating the movement of fluids through the flow channels (see [0068] and [0069]).

The method disclosed by the reference comprises the steps of introducing a reagent into the first flow channels such that the reagent binds to the ligands immobilized to the surface of the solid substrate, and then introducing a sample solution into the second flow channels such that the sample in the sample solution circulates through the flow channels and binds the reagents bound to the immobilized ligands (see claims 25 and 26). The reference discloses that the limitation "reagent" refers to oligonucleotides, peptides, monomers, and other small molecules that are building blocks of a larger molecule (see [0056]). While the fluid is being introduced into one of the two flow channels, the other set of flow channels is closed off by means of the control valves in order to prevent cross-contamination (see [0089]). The reference also discloses that reagents/samples that do not bind to the substrate are rinsed off using a solvent (see [0084]). The efficacy of the binding is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence (see [0122]). The method disclosed by Van Dam et al. differs from the claimed method in that Van Dam et al. do not disclose the step of manipulating the valves to form a closed loop.

Quake et al. disclose a microfluidic device similar to the device disclosed by Van Dam et al. Like the device disclosed by Van Dam et al., this device comprises intersecting microfluidic channels and elastomeric valves. Quake et al. also disclose a method for detecting analytes, the method comprising the steps of hybridizing a sample with probes immobilized to the surface of the microfluidic channels. Quake et al. also disclose the step of manipulating the valves to form a closed loop of flow channels. The closed loop enables the sample to circulate throughout the loop and properly hybridize with the probes (see Abstract and [0076]). Quake et al. also disclose the step of incubating the reaction to enable proper hybridization (see [0310]). In light of the disclosure of Quake et al., it would have been obvious to one of ordinary skill in the art to manipulate the valves of the Van Dam et al. device to form a closed loop of channels during the hybridization step to ensure that the sample and the reagents properly hybridize. It also would have been obvious to incubate the reaction to ensure proper hybridization.

With respect to claims 23-26, Van Dam et al. disclose the step of derivatizing the solid substrate and determining the efficacy of the derivatization (see [0122]). This is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence. In light of the disclosure, it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method described above and detect the fluorescence using a fluorescent microscope in order to observe the efficacy of the synthesis.

With respect to claim 31, given that the device disclosed by the Van Dam reference is adapted to perform binding assays, it would have been obvious to one of ordinary skill in the art to react any two entities that bind using the device disclosed by Van Dam et al., including a cell as the reagent and antimicrobes as the sample in order to observe the effects of the antimicrobes on the cell.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. in view of Quake et al. as applied to claims 14, 15, 18-26, 28-31 and 34-37, and further in view of Raillard et al. (US 2002/0102577 A1).

Van Dam et al. does not explicitly disclose the usage of a non-optical detector to observe the compound synthesis.

Raillard et al. disclose a method for labeling probes with radio-isotopes that emit radiation (see [0132]). The probe is detected using a detector that is sensitive to radiation.

In light of the disclosure of Raillard et al., it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method disclosed by Van Dam et al. with radio-isotope probes instead of fluorophores and detect the radiation using a detector in order to observe the efficacy of the synthesis in the event that fluorophores are not available.

Response to Arguments

Applicant's arguments with respect to the art rejections have been fully considered but they are not persuasive.

First, Applicant argues that the cited references do not provide a motivation for modifying the method disclosed by Van Dam et al. Specifically, Applicant argues that Van Dam et al. disclose a method wherein fluids are introduced at one end and expelled at the opposite end. Because the reference only discloses fluid flow in a single direction, Applicant argues that there is no motivation to form a closed loop. This argument is not persuasive. Van Dam et al. disclose that more complicated reaction sequences can be achieved by closing the valves leading to waste, which has the effect of redirecting fluid flow into another channel flowing in the opposite direction (see [0190]). The disclosure provides motivation for redirecting fluid flow, and combining said disclosure with the disclosure of Quake et al. provides sufficient motivation for forming a closed loop flow by manipulating the valves.

Applicant also argues that manipulating the valves of the Van Dam et al. device to circulate the fluid into another channel would increase the time required to perform synthesis, which would decrease the utility of the device. This argument is moot in light of the motivation provided by Van Dam et al. Specifically, Van Dam et al. disclose that the sample fluid can be redirected into other channels thereby circulating the fluid sample throughout the entire fluid network. Based on the disclosure, the problem identified by Applicant appears to be moot.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL S. HYUN whose telephone number is (571)272-8559. The examiner can normally be reached on Monday-Friday 8AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Paul S Hyun/
Examiner, Art Unit 1797

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797